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Building a job-exposure matrix for early plutonium workers at the Sellafield nuclear site, United Kingdom

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Abstract

The potential for adverse health effects from internal exposure to Plutonium has been recognised since its discovery in the 1940s. However, in the absence of specific information, potential risks from Plutonium exposure have always largely been controlled through knowledge of radiation exposure risks in general, much of which comes from external radiation exposures. To try to obtain more direct estimates of potential internal exposure risks, epidemiological studies of Plutonium workers need to be conducted. Such epidemiological analyses require individual Plutonium exposure estimates that are as accurate and unbiased as possible. The UK Sellafield workforce includes one of the world's largest cohorts of Plutonium workers, which constitutes, by some considerable margin, the group of workers most comprehensively monitored for internal exposure to this alpha-particle-emitter. However, for several hundred workers employed at the start of Plutonium work at the

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facility, during the period from 1952 through to 1963, the historical urinalysis results available cannot provide sufficiently accurate and unbiased exposure assessments needed for use in epidemiological studies. Consequently, these early workers have had to be excluded from epidemiological analyses and this has significantly reduced the power of these studies. A promising quantitative methodology to overcome the issue of missing or deficient exposure data, is to use exposure data from other sources to estimate the average exposure a 'typical worker' would have received, and to collate this information for specific occupations and years. This approach is called a Job-Exposure Matrix (JEM). Work on a pilot study to construct a population-specific quantitative JEM for the early Plutonium workers at Sellafield during 1952–1963, for whom reliable urinalysis results do not exist, has shown the potential for a JEM approach to produce more reliable and useful exposure estimates for epidemiological research.

Supplementary material for this article is available [online](#)

Keywords: radiation, radiation workers, job-exposure matrix, JEM, exposure assessment, plutonium

(Some figures may appear in colour only in the online journal)

Introduction

Plutonium has been recognised as a human health hazard since the 1940s; primarily because its main isotopes undergo radioactive decay through alpha particle emission [1].

Epidemiological analyses of populations exposed to ionising radiation have the potential to directly investigate any health effects of such exposures. Historically, most epidemiological studies have largely been concerned with exposures to highly penetrating photon radiation (i.e. gamma and x rays) with sources external to the body, because such exposures are more common and much easier to evaluate than doses from internally deposited radionuclides. However, owing to its high linear energy transfer rate, alpha particle radiation exhibits significantly enhanced biological effects at the cellular level relative to gamma radiation, so there is also a specific need to investigate the health risks of exposures to alpha particle emitters such as Plutonium. Exposure to Plutonium, as encountered by workers in the nuclear industry, especially historically, has been associated with increased risk of lung cancer [2], but there are large uncertainties on these risk estimates; a major component of which arises from issues with Plutonium exposure assessment, particularly for early workers.

The Plutonium worker cohort at the Sellafield site (originally Windscale Works) in the North-West of England is one of the largest and longest standing cohorts of this type in the world. Sellafield was originally constructed to supply Plutonium for military purposes; production of which started in February 1952. Operations later increasingly focussed on the reprocessing of civil nuclear fuel and from 1971 the, greatly enlarged, site (then known as Windscale and Calder Works) was managed by British Nuclear Fuels Ltd (BNFL) and in 1981 renamed Sellafield. The production of Plutonium requires the reprocessing of uranium-based nuclear fuel, involving the chemical dissolution of irradiated fuel to separate out any Plutonium, remaining uranium, and waste fission products in the fuel; the separated

Plutonium is then purified in ‘finishing lines’. During this process there has been the potential for workers at Sellafield to be exposed to Plutonium; primarily through inhalation.

The Sellafield Plutonium worker cohort has been the subject of previous epidemiological analyses [2–5], which revealed particular issues with exposure assessments for workers during the period 1951 to 1963 [6–8]. These early exposures were originally controlled on the basis of the assumption that there was a threshold level for total Plutonium intake below which there would be no adverse health effects, known as a ‘Maximum Permissible Body Burden’ (MPBB) [9]. This assumption resulted in monitoring and record keeping decisions which have made retrospective Plutonium dose assessment problematic, and as a consequence it has not been possible to produce a reasonable dose assessment for these workers.

Early operational protection measures were simply based on a threshold level of urinary Plutonium excretion, known as the ‘Reporting Level’ (RL) [10]. Excretion less than the RL would indicate a maximum intake which was a conservatively ‘safe’ fraction of the MPBB irrespective of any assumptions regarding exposure. Further action to investigate and control an individual’s Plutonium intake was only considered necessary if excretion was above the RL. Consequently, the actual Plutonium content of urine sample results that were less than the RL was unimportant and these results were often only recorded as being less than the RL value (<RL). This system was sufficient for operational protection purposes at the time, as it controlled the risks to those who were exposed. However, radiation protection systems have since evolved and are now underpinned by the assumption that there is no exposure threshold for the induction of stochastic health effects such as cancer.

Epidemiological research into Plutonium exposure risks requires such exposures to be assessed down to as low a level as technically possible. Urinalysis results are now used with sophisticated biokinetic models of Plutonium absorption, distribution, metabolism and excretion, in conjunction with statistical fitting techniques, to estimate an individual’s Plutonium intake(s) over time. These Plutonium intake values and biokinetic models can then be used with dosimetric models to estimate specific organ and tissue doses for epidemiological analyses. The assessed intakes, and hence doses, for individuals within an epidemiological study are directly correlated to the recorded level of Plutonium in their urinalysis results. Consequently, the minimum dose which can be resolved from censored urinalysis results (i.e. those that are only recorded as being less than some value), for example <RL, is directly correlated to the censorship level. The RL used for early urinalysis results, approximately 46 mBq⁶, was some 20 times higher than the contemporary analytical detection limit and 100 times higher than that for later samples. However, for a proportion of early workers records their actual analytical results still exist, and from these it can be seen that their true urinary excretion was well below the RL and often below the limit of detection. It is evident that the minimum doses that can be assessed for early Plutonium workers with only <RL results will greatly exceed those for other workers, particularly those with later urinalysis results, and also the likely true doses for most workers at the time. Consequently, dose estimates solely based on <RL results cannot reasonably be used within epidemiological analyses, and the 630 Sellafield workers with such results have had to be excluded from previous analyses of the cohort. This reduction in the number of workers in the cohort significantly reduces the statistical power of epidemiological studies to investigate exposure risks, while in addition these ‘early’ workers are amongst the most informative with regard to Plutonium exposure risks.

⁶ This RL value for early urinalysis results is an approximation because the original limit was actually framed as being less than 20 μg (*sic*—i.e. pg) of Plutonium per sample and the equivalent alpha activity has to be inferred based on assumptions about the isotopic content.

In an attempt to address this issue a pilot study to explore the use of an alternative, group-based methodology for retrospective exposure assessment, the Job Exposure Matrix (JEM) [11], was conducted to enable estimation of Plutonium intakes for this early-worker sub-cohort. The JEM approach is a standard exposure assessment methodology for epidemiological studies of chemical and physical occupational exposures [12], and involves the estimation of the average exposure level a typical worker in a homogenous exposure group would have received in a given time period, assuming that the exposures of individual workers in the same group (often described by the job/occupation) come from the same distribution [11]. The advantage of this group-based exposure assessment is that for workers with missing exposure information, their average exposure can be estimated for use in an epidemiological study (although of course the individual exposures within a group will differ), and that these estimates are primarily subject to Berkson errors, which lowers the statistical power but generally does not bias results, rather than classical measurement error [13, 14]. Although, if there are sufficient reliable exposure data available, a quantitative JEM is generally preferable, in the absence of sufficient quantitative exposure and contextual data, a hybrid approach, in which quantitative data and expert judgment are combined, can also be used [15]. Given that reasonable urinalysis data were available for some of the early Sellafield Plutonium worker cohort, we followed the latter strategy and combined the available quantitative exposure (urinalysis) data with information on occupations, work areas/processes (activities and materials used at the workplace), along with any relevant associated temporal information (e.g. dates of employment).

The aim of this study was to demonstrate that a JEM approach can be used to produce more reliable Plutonium intake estimates, which can then be used to generate sufficiently reliable doses to permit data for workers with all <RL urinalysis results to be included in future epidemiological research. Here we describe the strategy and processes used for building a JEM for early Sellafield Plutonium workers and present the JEM which was developed. Assessment of the accuracy and precision of this JEM and its sensitivity to decisions made in the exposure assessment is described elsewhere [16].

Methods

Data sources

The primary sources of information on which the JEM is based were the relevant data systems (see the following) operated by Public Health England and at Sellafield Limited. As part of the Corporate Epidemiological Database System (CEDS) for the former British Nuclear Fuels Limited (BNFL) worker cohort, Public Health England (PHE) manages a database of more than 485 000 urinalysis results for the group of approximately 12 500 Sellafield Plutonium workers monitored between 1952 and 2006. The Sellafield Approved Dosimetry Service (ADS) holds the primary sources of Plutonium urinalysis results for these workers, including some original paper records for pre-1990s results. Employment histories are available as a mixture of paper and electronic records. Finally, the Sellafield ADS also has access to individual dossiers for monitored individuals which hold a variety of paper records. Prior to the start of JEM building, potential issues such as missing data, ambiguous values, or potential duplicate entries in these data were identified, and the Sellafield researchers went back to original dosimetry and personnel (human resources) records to resolve these queries. A list of the data variables used in the JEM building process is provided in supplementary appendix A.

It should be noted that all personal identifiable and other sensitive data were only handled by Public Health England and/or Sellafield staff with the relevant responsibilities. Only appropriately anonymised data were handled by other members of the research team. University Research Ethics approval was obtained by the University of Manchester (reference number TPS170214). Further approval was obtained from the NDA-PHE Epidemiology Governance Group, which provides independent governance and oversight of epidemiological research proposed or undertaken in relation to workers of the former BNFL sites, which include Sellafield.

Study population

The identified early-worker sub-cohort for which this JEM was being built, labelled ‘JEM cases’ henceforth, comprised Plutonium workers who were employed at Windscale Works between 1 January 1952 and 31 December 1963, and for whom the only urinalysis data available were recorded as being <RL with no quantitative measurement. 1952 was selected as the start year because records show the first Plutonium production plant began operating in February 1952 (for the ‘the Hurricane Run’) [17]. Although it might be possible that some very small quantities of Plutonium could have been available at Sellafield in 1951 for research and development purposes, there would not have been any possibility of significant widespread exposure prior to the reprocessing plant opening in 1952. While it was believed that the practice of only recording results as <RL had been phased out in 1961 [10], the last year for this sub-cohort was specified as 1963 because some workers appeared to have such records up to this year. Using these criteria, 630 individuals were identified and included in this study.

These 630 workers had a total of 81 job titles and were associated with 61 work groups (an internal classification based on location, process or task, department and cost centre) during the period of interest. An expert panel, who had extensive knowledge of industrial processes at the Sellafield site and also Plutonium exposures and monitoring over time, (AR, RW, CW and MP) was assembled from within the research team. The expert panel concluded, after reviewing all available information, that ‘work group’ rather than ‘job title’ was the most accurate proxy for exposure, and therefore further matching of ‘JEM cases’ and ‘exposure analogues’ (see the following) was done on this basis.

Building a JEM based solely on occupational information has been the common approach for workers with internal radiation exposures [15], while quantitative exposure data has previously only been used once in a tritium JEM for employees at the US Savannah River Site [18], reflecting the difficulties associated with exposure assessment in this industry. A particular difficulty of developing a quantitative JEM for Plutonium workers, which makes it fundamentally different from the development of most other JEMs (e.g. for chemical or tritium exposures), is that internally deposited Plutonium is retained in the body long-term (i.e. many years). Therefore, it is generally not possible to simply impute average exposure just using urinalysis data for all workers employed in a specific area in any given year, as an individual’s excretion reflects any previous exposures in other areas and/or previous years. To resolve this difficulty, we devised an alternative and novel methodology to be able to obtain quantitative exposure estimates, and used a set of ‘exposure analogues’.

These ‘exposure analogues’ are Sellafield Plutonium workers matched to ‘JEM cases’ as follows: they had worked in the same work group over the same period of time as the ‘JEM cases’, this also had to be their first job in the industry (so that retention of Plutonium from previous exposure was not an issue), and they had quantitative urinalysis data (censored only by the relevant analytical limit at the time) available. In total 330 such ‘exposure analogues’

were identified. The original laboratory urinalysis results for these workers were held on paper records in various different locations for decades because they were considered of secondary importance. As a result not all records have survived until now, but there is no reason to suspect that the availability of these more reliable records for any specific individual is anything other than random. Consequently, the use of these exposure analogues should provide unbiased estimates of average exposures.

The identified data sources represented the entirety of all available urinalysis data, and it was recognised that they would have to be used for both building and validating the JEM [19]. Therefore, prior to building the JEM, the dataset was split into two separate data sets using a random allocation algorithm: 90% of the data (574 JEM cases and 280 analogues) were used for building the JEM and 10% (56 JEM cases and 50 analogues) were kept for internal cross-validation purposes (described elsewhere [16]).

Homogenous exposure groups

Pre-screening of work history information showed that the JEM cases had worked in a total of 85 different work groups during the 1952–1963 period. However, it was apparent that some of these groups were involved in activities with no potential for Plutonium exposure, others were involved in work with similar potential for exposure, activities and potential for exposure in some groups had changed significantly over time, and some individuals had missing work group information within the period of interest but had been monitored for exposure. A further issue was the very limited ‘data budget’ (i.e. the number of reliable urinalysis results for individuals who had no previous exposure in another group) available for quantitative assessment of exposures and the need to ensure that this was not spread too thinly across an unnecessarily large number of exposure groups, otherwise group average exposures would be poorly characterised. Hence, these 85 work groups were evaluated using quantitative⁷ and qualitative (expert assessment) methods to address these issues and thereby identify a final set of distinct exposure groups which covered all key potential routine Plutonium exposure scenarios within the period of interest. Further details of this evaluation process are provided in supplementary appendix B, but, in summary, this was an iterative process, involving multiple reviewing rounds, to refine the final exposure groups and to try to ensure there would also be sufficient information to produce reasonable average annual intake estimates for each of these groups. During this process, an additional ‘general exposure group’, for individuals for whom specific work group information was not available, was created. Work groups with similar names and job descriptions or for which average intakes would not materially differ from other groups (based on the quantitative information available i.e. distributions, central tendencies and variability of urinalysis results) were combined. Where work groups had multiple distinct periods of operation involving significantly different potential for exposure they were split into separate sub-groups (indicated by a sequential alphabetic suffix) and thereafter reviewed independently. Any groups with no apparent potential for exposure on the basis of urinalysis records (e.g. without measurements above the analytical detection limit after removal of anomalous urinalysis results) or where the expert panel, having reviewed all available information, concluded that there had been no real possibility of intake, were removed.

This process resulted in a final set of 14 discrete groups with the potential for Plutonium exposure in the 1952–1963 period, within which at least one JEM case had worked and for

⁷ Note that JEM cases were included in this analysis dataset because, although their data alone cannot provide reliable intake estimates, it can provide additional information for JEM development when combined with the data for the analogues and then analysed with statistical techniques suitable for use with censored data.

Table 1. Description of the final JEM groups.

JEM group name (code)	Description
General group	General default ‘background’ intake level for JEM cases for whom we have no group information, but who are likely to have had some exposure.
Plutonium Finishing (ZC04)	Plutonium finishing plants
Health Physics & Safety (Z005)	Health Physics and Safety, e.g. contamination monitoring
Non-scientific Research and Development (Z011)	Graphite workshop, Chemical Services Dept., Chemical Group analysts
Plutonium Recovery (ZC15)	Plutonium purification plant, thermal denitration plant, Plutonium recovery plant
Mechanical Maintenance (Z016)	Plant maintenance work in the separation area
Research and Development (ZC20)	Chemical Services (senior staff), Construction Services, technical branch, Chemical Inspectorate, Works/Secretariat staff, Research and development branch, Reactor Group personnel, Training Dept. staff, Chemical Services
Instrument Maintenance (ZC24)	Separation/Central instrument maintenance, Instrument maintenance main & pile
Training (ZC31)	Training, apprentice training
Plant Maintenance and Construction (ZC36)	Electronic instruments, Plant maintenance construction, Building works/central engineering dept.
Primary Separation Process (Z039)	Primary Separation Process
Electrical Maintenance Main (Z042)	Electrical Maintenance Main
Decontamination Centre (Z075)	Decontamination Centre
Laundry (Z076)	Laundry

whom the available evidence implies exposure comes from a single distribution. Some JEM cases had been employed in work groups other than these final 14 exposure groups, but based on expert judgment and available quantitative measurement data this particular work was very unlikely to have had real potential for non-trivial Plutonium exposure (supplementary appendix B). The final 14 exposure groups, for which Plutonium intakes estimates were to be produced for the final JEM, and a general description of them, are presented in table 1.

A total of 4487 annual work records were used as input to construct the JEM. The total number of individual group-year work history records that fed into the estimates of each of the JEM groups is shown in supplementary appendix C.

Estimation of Plutonium intakes

The 4487 annual work records used as input for the JEM were linked to 6899 relevant contemporary urinalysis results⁸, this being a 90%, randomly selected, subset of the results which were identified as being suitable for building and validating the JEM (i.e. linked to potential Plutonium exposure in a single work group and which were provided by individuals with no known previous exposure elsewhere). The distribution of these urinalysis samples across work groups and years is shown in table 2.

⁸ Note that because acute exposure events are, and have always been, relatively rare and non-routine, urinalysis results associated with them were not included in any part of this analysis including the calculation of Plutonium intakes for the final JEM groups.

Table 2. Distribution of urinalysis results, by work group and year, in a 90% random sample used to build the JEM.

Group/ Year	1952	1953	1954	1955	1956	1957	1958	1959	1960	1961	1962	1963	Total ^a
general	58 (41)	222 (162)	204 (189)	116 (100)	29 (24)	29 (16)	13 (5)	33 (25)	30 (17)	52 (12)	140 (61)	237 (108)	1163 (760)
ZC04	2 (2)	16 (13)	22 (22)	4 (4)	3 (3)	9 (7)	4 (1)	27 (12)	46 (5)	119 (17)	186 (22)	156 (34)	594 (142)
Z005	47 (30)	112 (46)	65 (50)	51 (30)	20 (13)	31 (18)	24 (9)	39 (19)	41 (10)	134 (13)	476 (92)	157 (36)	1197 (366)
Z011	0 (0)	1 (1)	5 (5)	9 (7)	11 (10)	1 (1)	2 (1)	8 (2)	6 (1)	8 (0)	18 (4)	0 (0)	69 (32)
ZC15	6 (3)	48 (13)	37 (24)	15 (11)	0 (0)	5 (2)	6 (2)	14 (7)	2 (1)	2 (0)	0 (0)	0 (0)	135 (63)
Z016	18 (10)	120 (52)	144 (104)	107 (70)	36 (13)	30 (19)	33 (13)	22 (7)	12 (1)	66 (5)	122 (21)	150 (29)	860 (344)
ZC20	30 (19)	180 (141)	230 (213)	137 (127)	33 (26)	51 (39)	59 (37)	66 (46)	29 (10)	70 (12)	268 (112)	430 (128)	1580 (910)
ZC24	8 (8)	22 (21)	29 (27)	5 (4)	8 (6)	11 (7)	23 (10)	4 (2)	13 (5)	18 (2)	23 (8)	50 (11)	214 (111)
ZC31	0 (0)	1 (1)	7 (6)	6 (6)	8 (8)	3 (3)	0 (0)	1 (1)	3 (1)	3 (2)	0 (0)	7 (0)	39 (28)
ZC36	0 (0)	18 (13)	78 (68)	49 (41)	11 (4)	21 (6)	23 (6)	19 (5)	25 (14)	25 (7)	55 (21)	22 (8)	346 (193)
Z039	11 (8)	58 (37)	54 (42)	28 (21)	17 (6)	19 (9)	2 (0)	3 (1)	4 (0)	1 (0)	37 (3)	24 (9)	258 (136)
Z042	3 (3)	11 (11)	17 (17)	18 (18)	19 (19)	7 (7)	6 (6)	11 (8)	7 (6)	2 (0)	9 (2)	2 (1)	112 (98)
Z075	0 (0)	0 (0)	1 (0)	9 (2)	14 (7)	12 (8)	30 (16)	3 (0)	9 (5)	28 (5)	43 (9)	81 (12)	230 (64)
Z076	0 (0)	0 (0)	1 (1)	0 (0)	1 (1)	0 (0)	0 (0)	0 (0)	0 (0)	11 (1)	45 (13)	41 (19)	99 (35)
Total ^a	183 (124)	809 (511)	894 (768)	554 (441)	210 (140)	229 (142)	225 (106)	250 (135)	227 (76)	539 (76)	1422 (368)	1357 (395)	6899 ^b (3282)

^a total number of urinalysis results (in the bracket is total number of censored urinalysis results).

^b for the 100% of individuals, the corresponding totals are 8082 and 3783, respectively.

Grey cells: >75% of measurements below the Limit of Detection (LOD).

The JEM ‘build’ urinalysis dataset was used as the input to a modified version (‘PumaXJEM’) of the ‘PuMA’ Plutonium mass assessment code [20] to produce a set of initial annual intake estimates for each of the final JEM groups across the period of interest. PumaXJEM uses mathematical models of Plutonium absorption, distribution, metabolism, and excretion to assess intakes and doses. The underlying methodology is based on the International Commission on Radiological Protection (ICRP) Publication 130 Human Respiratory Tract Model [21] and the revised ICRP Publication 67 [22] systemic model for Plutonium developed by Leggett *et al* [23]. The overall methodological approach employed was based on that used for the SOLO project (including the same Sellafield Plutonium nitrate absorption parameters: $f_r = 0.17$, $s_r = 1.0$; $s_s = 0.0022$; $f_b = 0.002$, $s_b = 0.0$, and $f_1 = 0.0001$); a joint epidemiological analysis of Plutonium workers at Sellafield and the Russian Mayak facility funded by the European Union 7th Framework Programme [8]. However, PumaXJEM uses Maximum Likelihood Estimation (MLE) instead of Bayesian estimation (as used for SOLO) to avoid potential bias resulting from a relatively ‘strong’ intake prior with potentially ‘weak’, heavily censored, data. Powell’s (optimisation) method [24] is used to derive the intake values which would best explain the relevant urinalysis observations. The initial unadjusted, ‘raw’, intake results produced by PumaXJEM are presented in supplementary appendix D (table D1).

It was recognised that, although 6899 urine samples informed the building of the JEM overall, the number of available urinalysis results varied widely between cells (see table 2), and hence the reliability and precision of the derived intake estimates for any specific group-year would also vary significantly. To investigate the validity and reliability of the initial intake estimates that had been produced, summary statistics were generated for the final ‘build’ urinalysis data set on which they were based using the NADA package [25] in the R language and environment for statistical computing and graphics [26]. The NADA package permits summary statistics to be produced for heavily censored data with multiple levels of censorship (in this instance the reporting level and analytical LODs for urine measurements) using different statistical methods: MLE (as used within PumaXJEM), Regression on Order Statistics, and Kaplan-Meier statistics for non-parametric analyses. These summary statistics showed that distributions were significantly skewed (means were positively shifted with respect to median values) and that for some group-year combinations there was insufficient information (e.g. small number of samples and/or very high percentage of censored results) to produce reliable central estimates of urinary excretion and hence intake: The unreliability of data was often readily indicated by the NADA package being simply unable to produce a median excretion value in some instances, and in others there were significant discrepancies in the median⁹ values produced by the different statistical methods within the package.

Another issue was that some of these initial Plutonium intake results were known to be potentially subject to significant bias as they were based on urinalysis monitoring records for the earliest years, 1952–53, which are known to be the most unreliable. To mitigate the impact of these earliest urinalysis measurements, Plutonium excretion values in the years following 1953 for each sub-group of workers who had worked in one of the JEM group in 1952–53, were compared to those for the group overall and to those for workers who had only worked in that JEM group from 1954 onwards. In the case of significant differences, an intake ratio factor was calculated so that pre-1954 intakes could then be derived from intake

⁹ Median values were used as they represent the geometric mean of a log-normal distribution, the distribution assumed for urinalysis data within PumaXJEM, they are also the most robust and, hence directly comparable, central estimators produced by all the three methods used within the NADA package.

estimates for later years, which are based on comparatively more reliable data, through these factors.

Using the results of the above intake ratio analysis, the information on the reliability of the remaining raw intake values from the summary statistics for the urinalysis data on which they were based, and expert judgement, all JEM cells were systematically reviewed; a 'mask' was produced showing which elements of the Group/Year intake matrix were reasonably reliable and those that were not (see supplementary appendix D, table D2).

The intake values that corresponded to the elements of the above mask that were considered reliable, including all those indicating no exposure, were directly transcribed to the final JEM. Further analyses were then conducted to determine approaches that could be used to modify or substitute each of the remaining intake values (i.e. those which were considered unreliable) to produce values which better reflect the potential true intake for inclusion in the final JEM. The approaches which were ultimately used included intake ratio factors for early years (see the aforementioned), extrapolation, interpolation or substitution (using more reliable intake values from the Group/Year intake matrix) and, where no other option was available, expert judgement (see supplementary appendix D, table D3). While the majority (i.e. 119 out of 168) of intake values in the final JEM remained unchanged, the modified intake values differ from the initial unadjusted raw intakes by factors ranging from 0.1 to 4.0 (see supplementary appendix D, table D4).

Results

The final intake estimates which were derived for the early Sellafield Plutonium worker JEM are shown in table 3.

These average annual Plutonium intakes (in Bq) supplied by the JEM were subsequently used to estimate the 1952–1963 cumulative intake for each of the 630 'JEM cases'. To take into account workers having had multiple jobs in one year and/or not having worked for the full year, annual intakes were first converted to daily intake rates in Bq/day, obtained by dividing each annual JEM estimate by the number of days in that year. These daily intake rates were then multiplied by the number of days a worker had worked in that particular JEM group during that year, with all such exposures for that worker being summed to derive their total 1952–63 cumulative intake. For the purposes of comparison, cumulative intake estimates for the JEM cases were also produced using traditional internal dose assessment methodology (using the same underlying biokinetic models and parameters) and the relevant unadjusted individual urinalysis data (where the last sample for an individual is assumed to be positive at the reporting level in order to fit a constant chronic intake to all of their results), and a direct comparison is provided in figure 1.

JEM-derived cumulative individual Plutonium intakes range from 'no intake' to 990 Bq, with mean and median cumulative individual intake being 112 Bq and 95 Bq, respectively, while the traditional methodology produced cumulative intake estimates ranging from 534 to 36 700 Bq, with mean and median cumulative individual intake being 5843 Bq and 4668 Bq, respectively. The intake estimates produced by the JEM are much more credible and in keeping with other information about the possible magnitude of exposures for these early workers, as based on the fact that (1) the missing urinalysis reports for these workers was assumed to be due to chance alone (as discussed previously), and (2) if the original high estimates in figure 1 were correct then deterministic health effects would have been observed in routine medical surveillance of workers at the time, which was not the case.

Table 3. The final Plutonium intake Job-Exposure Matrix (in Bq).

Group/Year	1952	1953	1954	1955	1956	1957	1958	1959	1960	1961	1962	1963
General	50	50	30	40	40	45	60	70	105	60	30	15
ZC04	40	40	30	40	40	85	135	205	175	85	50	40
Z005	65	65	40	50	50	70	100	130	175	50	45	30
Z011	0	0	0	40	40	45	60	70	90	40	35	0
ZC15	70	70	45	25	0	40	35	90	90	90	0	0
Z016	110	110	65	45	70	45	100	165	125	170	65	30
ZC20	55	55	40	30	65	30	70	35	100	40	30	25
ZC24	55	55	35	20	20	20	105	110	115	90	45	50
ZC31	90	90	45	40	40	45	0	70	105	60	0	30
ZC36	85	85	45	35	45	90	60	120	125	35	25	20
Z039	95	95	60	25	45	30	80	100	30	55	115	15
Z042	55	55	45	45	60	85	75	90	45	45	45	5
Z075	0	0	40	40	45	35	70	65	65	60	60	35
Z076	0	0	40	0	40	0	0	0	0	65	40	10

Note: Intake estimates have been rounded to the nearest 5 Bq to better represent the likely true precision of these results.

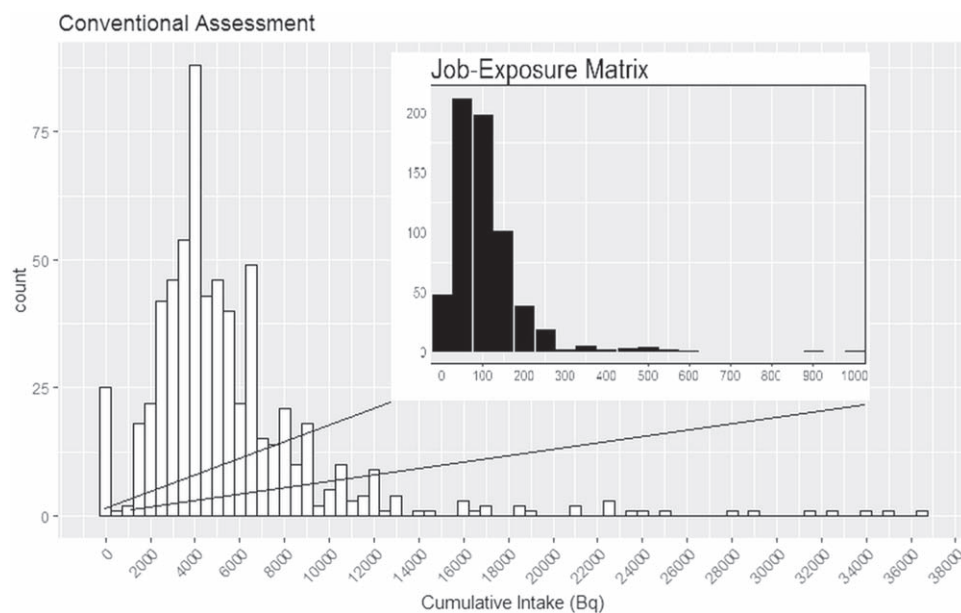


Figure 1. Histograms of cumulative individual Plutonium intakes (Bq), 1952–1963, for the 630 JEM cases using the JEM and conventional assessment methods.

Discussion

A review of the literature had shown that Plutonium exposure estimates in the nuclear industry from JEMs had initially been largely empirical and based solely on expert knowledge of likely exposure conditions, but that more recently there had been a move to base exposure estimates, either entirely or in part, on more quantitative measures [15]. The use of a hybrid approach to JEM building for this study has proven to be successful and has generated much more credible intake estimates, which will likely be useful in epidemiological research that up to now has had to discard data for workers whose exposure assessment relied (whole or in part) on these early and unreliable intake assessments. Complementary cross-validation and sensitivity analyses provide further evidence that the JEM provides credible and reasonably accurate and robust estimates for annual Plutonium intakes in this period [16]. Moreover, the use of ‘exposure analogues’, as developed in this study, provides a novel methodology that enables the development of a population-specific job-exposure matrix for protracted Plutonium exposure using standard JEM-building methods that could previously not be directly transferred from their use in other industries.

Several other factors were considered for inclusion in the construction of the JEM, but eventually were not, or could not, be included. Specifically, the use of chelation therapy or chelating agents was not included because these were rarely used in practice. Although they were used for a small number of potentially large acute exposures at Sellafield, such acute exposures are not representative of routine exposures within a group of workers, which tend to be low level chronic in nature, and thus would skew estimates of central tendency. Furthermore, the possibility of including personal or static air sample results to supplement urinalysis data would have been beneficial, but investigation of the availability of such information indicated that these data did not exist for the relevant years. Historical static air sampling monitoring data were not available for Sellafield, while routine personal air

sampling for Plutonium was only introduced at Sellafield in 1985, and as such would also not provide additional input data that could supplement the early-years JEM.

A further decision was made to develop the JEM for average annual Plutonium intakes in Bq and not for organ/tissue absorbed doses in gray (Gy), which is the general metric used in epidemiological studies. The organ doses an individual receives in any specific year reflects the sum total of all their previous intakes, not just their intakes in that year (unless it happens to be the year of their first and only intake) and doses also continue to be received for many years following cessation of intake. Another important reason for taking this approach was that it allows future users of the JEM to make different assumptions with respect to, for example, Plutonium solubility to calculate absorbed doses. The advantage of this is that whereas a static JEM could potentially become irrelevant in future if our scientific knowledge about these parameters changes, the current JEM can easily be adapted with updated solubility parameters. The downside of this approach however, is that it makes usage of the JEM less straightforward because additional individual-level dose assessments based on intake patterns will be required prior to epidemiological research, although this is also the case for conventional internal dose assessment when methodology is revised.

There are some limitations to the final JEM. Although the MLE technique used combines the probabilities for both censored and uncensored observations and is fairly robust, even when the percentage of censored results is relatively high, the optimisation method cannot produce an intake estimate other than zero if all the urinalysis results associated with that intake are censored (this being the minimum intake value that best describes such data). To deal with completely censored data the PumaXJEM algorithm assumes that the last sample is uncensored and calculates the intake on this basis, but obviously the resulting intake value represents an upper limit estimate of the true intake rather than an unbiased central estimate; however, this issue also arises in conventional internal dosimetry which is similarly affected. Furthermore, the increased information on the timing and nature of exposures captured during the JEM building process means that periods when there is no likelihood of exposure are much less likely to be missed, this being evident by comparison of the distribution of results in figure 1.

Conclusion

With respect to epidemiological analyses, there are limitations in occupational radiation monitoring data, particularly for internally deposited radionuclides, such as Plutonium, in the early years of operation of the nuclear industry. The prototype hybrid JEM developed here shows the considerable potential for this technique to improve exposure estimates for early workers.

While the use of these JEM intake estimates for early Sellafield Plutonium workers is yet to be tested in an epidemiological study, it is likely that imputation of the missing exposures with JEM-derived values will have considerable impact on estimates. Early workers will usually have received some of the highest Plutonium exposures and, due to the passage of time, health outcomes for these workers will now be largely known.

Finally, the novel use of 'exposure analogues' developed in this study provides a generic methodological advance that is transferable to other Plutonium worker populations, and may contribute to the inclusion of 'early workers' that previously could not be included in other Plutonium worker cohorts.

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Competing financial interests declaration

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References

- [1] Brues A, Lisco H and Finkel M 1946 Carcinogenic action of some substances which may be a problem in certain future industries *United States Atomic Energy Commission Document No. MDDC-145 Abstract published in Cancer Research* 1947 **7** 48
- [2] Gillies M *et al* 2017 Lung cancer risk from Plutonium: a pooled analysis of the Mayak and Sellafield worker cohorts *Radiat. Res.* **188** 645–60
- [3] Grellier J *et al* 2017 Risk of lung cancer mortality in nuclear workers from internal exposure to alpha particle-emitting radionuclides *Epidemiology* **28** 675–84
- [4] Omar R Z, Barber J A and Smith P G 1999 Cancer mortality and morbidity among Plutonium workers at the sellafeld plant of British nuclear fuels *Br J Cancer* **79** 1288–301
- [5] Azizova T V *et al* 2018 An assessment of radiation-associated risks of mortality from circulatory disease in the cohorts of Mayak and Sellafield nuclear workers *Radiat. Res.* **189** 371–88
- [6] Bingham D *et al* 2017 Reconstruction of internal doses for the alpha-risk case-control study of lung cancer and leukaemia among European nuclear workers *Radiat Prot Dosimetry* **174** 485–94
- [7] Riddell A E *et al* 2000 The assessment of organ doses from Plutonium for an epidemiological study of the Sellafield workforce *J. Radiol. Prot.* **20** 275–86
- [8] Riddell T *et al* 2015 Deliverable 3.3.1: report on the development and validation of Plutonium dose assessment systems for epidemiological research. *European Union FP7 SOLO Report*
- [9] Beach S and Dolphin G 1964 Determination of plutonium body burdens from measurements of daily urine excretion *Int. Atomic Energy Agency, Assessment of Radioactivity in Man, II* (Brussels, Belgium: European Union) pp 603–15
- [10] Britcher A *et al* 1994 What do your Plutonium in urine results tell you? A tour through 40 years of change at sellafeld *Radiat. Prot. Dosim.* **53** 259–61
- [11] Hoar S 1983 Job exposure matrix methodology *J Toxicol Clin Toxicol* **21** 9–26
- [12] Teschke K 2003 Exposure surrogates: job-exposure matrices, self-reports, and expert evaluations *Exposure Assessment in Occupational and Environmental Epidemiology* ed N MJ (Oxford: OUP) pp 119–32
- [13] Kukush A *et al* 2011 Methods for estimation of radiation risk in epidemiological studies accounting for classical and Berkson errors in doses *Int J Biostat* **7** 15

- [14] Masiuk S V *et al* 2016 Estimation of radiation risk in presence of classical additive and Berkson multiplicative errors in exposure doses *Biostatistics* **17** 422–36
- [15] Liu H *et al* 2016 A review of job-exposure matrix methodology for application to workers exposed to radiation from internally deposited Plutonium or other radioactive materials *J. Radiol. Prot.* **36** R1–22
- [16] de Vocht F *et al* 2018 Construction, validation and sensitivity analyses of a job exposure matrix for early Plutonium workers at the Sellafield nuclear site, United Kingdom *Radiat. Res.* **191** 60–6
- [17] Gowing M 1974 *Independence and Deterrence: Britain and Atomic Energy 1945–1952. Policy Execution* vol 2 (London: Macmillan)
- [18] Hamra G, Nylander-French L A and Richardson D 2008 Dose reconstruction for an occupational cohort at the Savannah River nuclear facility: evaluation of a hybrid method *Radiat. Prot. Dosimetry* **131** 188–97
- [19] Stone M 1974 Cross-validatory choice and assessment of statistical predictions *Journal of the Royal Statistical Society Series B (Methodological)* **36** 111–47
- [20] Riddell A 2011 Development of an improved internal dose assessment methodology for Plutonium *Master of Philosophy Thesis* (Birmingham: University of Birmingham)
- [21] ICRP 2015 Occupational intakes of radionuclides: part 1. Publication 130 *Ann. ICRP* **44** 5–188
- [22] ICRP 1993 Age-dependent doses to members of the public from intake of radionuclides—part 2 ingestion dose coefficients. Publication 67 *Ann. ICRP* **23** 1–167
- [23] Leggett R W *et al* 2005 Mayak worker study: an improved biokinetic model for reconstructing doses from internally deposited Plutonium *Radiat. Res.* **164** 111–22
- [24] Powell M 1964 An efficient method for finding the minimum of a function of several variables without calculating derivatives *The Computer Journal* **7** 155–62
- [25] Helsel R 2012 *Statistics for Censored Environmental Data Using Minitab and R*. 2 edn (New York: Wiley)
- [26] R Core Team 2014 *R: A Language and Environment for Statistical Computing* (Vienna: R Foundation for Statistical Computing) (www.R-project.org/)